Risk Factors for Retinal Detachment

A Case–Control Study

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Objective: The aim of this study was to investigate risk factors for retinal detachment or tear (RD/T), and follow up two studies that found increased risk from work-related heavy lifting. **Methods:** We conducted a case–control study including 200 cases of RD/T and 415 controls. Participants completed a questionnaire covering general health, vision, and physical exertion. Multiple logistic regression and propensity score matching was used to control confounding and estimate independent effects. **Results:** RD/T risk was increased by one lifting measure: current regular lifting of more than 30 lbs (>13.6 kg). In the population aged less than 65 years, the odds ratio comparing those with/without heavy lifting was 1.81, 95% confidence interval = 1.08 to 3.04. **Conclusion:** Occupational heavy lifting may represent a risk factor for RD/T, but further research is needed in populations with frequent heavy physical exertion to more precisely quantify the risk.

Keywords: heavy lifting, myopia, obesity, retinal detachment, retinal tear

Retinal detachment (RD) is a potentially blinding pathology with an incidence of 5 to 20 cases per 100,000 person-years[1]; reasons for this variability are not well-understood. We investigated the most common type, rhegmatogenous RD, which occurs when liquefied vitreous passes through a retinal tear (RT) pulled open by tractional forces occurring as normal age-related vitreous shrinkage pulls the vitreous away from the retina.[2] Age, male gender, myopia, ocular surgery, and blunt force trauma to the head or eye are known risk factors for rhegmatogenous RD (hereafter called RD).[3]

Despite continuing improvements in treatment, complete recovery of visual acuity does not always occur, particularly if the macula is involved. A multicenter European intervention study reported that only 42% of postoperative cases achieved 20/40 or better vision.[4] In regions of the world without access to eye surgery, serious loss of vision still occurs.

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Retinal detachment (RD) is a leading cause of loss of visual acuity. This is the third study to report that occupational lifting may be a risk factor for RD. If this association were determined to be causal, it would provide additional motivation for implementing policies to reduce manual materials handling.

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In 2008, Mattioli et al[5] published one of the first epidemiologic studies designed to identify preventable RD risk factors. They hypothesized that heavy physical exertion, and specifically work-related heavy lifting, increased the risk of RD. Their Italian case–control study found evidence supporting this hypothesis; the principal finding was that study participants who reported a lifetime total occupational lifting history above the median value (8000 kg/week-years or 17,600 lb/week-years) had about a four-fold increase in risk of RD [odds ratio (OR) = 4.4, 95% confidence interval (95% CI) 1.5 to 13]. Mattioli et al also identified other risk factors for RD, including myopia, eye trauma, previous eye surgery including cataract extraction, and elevated body mass index (BMI). More recently, Farioli et al[7] found an increased risk of RD among men with a usual occupation involving heavy lifting in a large cohort of Swedish military conscripts followed for more than 40 years (relative risk = 2.38, 95% CI 1.15 to 4.93). Hypertension, obesity, manual labor, and oral fluoroquinolone use have also been recently proposed as possible risk factors by our team and others.[6–9]

To investigate further the hypothesis that physical exertion at work increases risk of RD, we conducted a case–control study designed to advance the evidence base in three ways: Increase statistical power with larger numbers of cases and controls; Gather more detailed information on physical exertion; and Use explicit *a priori* hypotheses to guide the choice of exposure measures and the interpretation of results. On the basis of our review of current understanding of the pathophysiology of RD, we hypothesized that, if heavy lifting is a risk factor for RD, risk is likely to be more strongly associated with the amount of heavy lifting in the current job than with lifetime measures such as total cumulative exposure or lifetime duration of heavy lifting.

METHODS

Study Design and Population

This prospective case–control study was conducted from September 2015 to December 2017. Incident cases were patients from a large comprehensive health care system serving central Massachusetts and from three independent retinology practices in the same catchment area. We included recent confirmed surgical repairs of either a RD or RT; the latter cases were included because tears frequently progress to detachments if not repaired.[10] Cases were identified through electronic medical records (EMRs) and insurance claims data using diagnosis (ICD 9 and ICD 10) and medical procedure codes (Appendix 1, http://links.lww.com/JOM/A731) to capture both RDs and RTs. Study control subjects were drawn from patients who were visiting the health care system's ophthalmology/optometry clinics throughout the same catchment area for routine eye examinations. All participants provided written informed consent following procedures that adhered to the guidelines of the Declaration of Helsinki and were approved by the Institutional Review Board of the University of Massachusetts Lowell.

Potential participants were identified weekly using the EMR database and telephone outreach to the independent retinology practices. For subjects identified through EMR, trained research nurses conducted manual chart reviews to confirm eligibility. Index dates for cases were the dates of their surgical repair and for controls the dates of their routine eye examinations. As several known risk factors could be eliminated in order to allow focus on our study factors, we excluded from the study patients who were ever diagnosed with diabetic retinopathy as well as those diagnosed with head, eye, or chest trauma or cataract surgery within the 3 months before their index date. Sufficient controls were randomly selected from eligible ophthalmology clinic patients to achieve a 2:1 control to case ratio.

Mailed Survey Questionnaire

Potential cases and controls were mailed a postcard notifying them that they would soon be receiving a survey packet related to a study of ‘‘eye health’’ in the mail. Patients were not aware of specific study hypotheses. The survey packet was mailed out two days later and included an introductory letter, two dollar bills as an incentive, a consent form, a survey, and a reference card with photographs of a person lifting, pushing, and pulling various objects as an aid to estimating weights lifted and the amount of effort needed for regular pushing and pulling. The introductory letter offered the patients the opportunity to participate by completing and mailing the forms or responding by telephone; they could also opt not to participate. Nonrespondents were followed up by telephone and a second mailing. Participants who completed the questionnaire were compensated $50 for their time.

The questionnaire included items on education, income, smoking and alcohol history, physical activity, housework, yardwork and hobbies, as well as both general and eye-related health. We also asked detailed questions about the lifetime occupational history.

Demographic and Health Variables

Age was calculated from month and year of birth and the index date. Race used the standard U.S. Census categories, but because less than 15% of participants were nonwhite, the variable was dichotomized into white/nonwhite. Education was trichotomized as high school or less, trade school or college, and more than college. There were four categories of annual household income: less than $25,000, $25 to $50,000, $50 to $100,000, and more than $100,000 (16% of respondents left this question blank or answered ‘‘prefer not to say’’). Smoking was defined as ever/never, and alcohol consumption as never, sometimes, and every day. BMI was calculated from self-reported current height and weight. For 76% of the participants, we also had EMR data on BMI and in these subjects, the clinical data agreed well with the self-reports ($r = 0.91$). A family history of RD was defined as self-report of a first or second-degree relative with RD. We recorded EMR-confirmed cataract surgery and when that was not available, used self-report of previous cataract surgery. We also asked about current use of high blood pressure medication because hypertension has been reported to be a risk factor for RD.[7]

Identifying Myopia

Myopia could be determined from recent refractive error data in the EMR for nearly all the controls but only 63% of cases. We therefore constructed a self-reported indicator of myopia, and assessed its accuracy in the 88% of participants for whom refractive error data were available. Information on myopia was collected using a validated set of five questions[11]: (1) Apart from sunglasses, have you ever worn glasses or contact lenses? (2) How old were you when you started wearing glasses? (3) What do you currently wear them for (seeing things clearly in the distance or seeing things clearly up close)? (4) How often do far objects appear fuzzy or not clear these days, when you are not wearing glasses or contact lenses? (5) Have you ever been told by an optician, doctor, or nurse that you suffer from myopia or near-sightedness?

Logistic regression was used to identify the best self-reported indicator of myopia from among these questions, with the gold standard defined as having negative refractive error less than –0.25 diopters in the worse eye. The Akaike Information Criterion (AIC) was used to select the best fitting model.[12] The best predictive model included only the question on age started wearing glasses, and the age that resulted in the best fitting model was before age 20. The sensitivity and specificity of this definition for identifying any degree of myopia were 58% and 76%, respectively. The sensitivity rose to 89% when tested for ability to identify moderate to severe myopia (refractive error $\leq$-3.0 diopters), although specificity declined to 65%.

Evaluating Heavy Physical Exertion

Occupational Exposure

Occupational exposure was assessed over the entire working life. Respondents were asked to list each job held for at least 20 hours/week for at least one year, providing the job title, the business name, the main product or service, and usual activities. Two expert raters evaluated each reported job (blind to case–control status) and assigned each to a six-digit Standard Occupation Code (SOC).[13,14] The two raters disagreed on the SOC codes of approximately 14% of the participants' jobs, and after joint review, a consensus assignment was made.

For each job, we extracted data from the US Occupational Resource Network (O*NET), of the U.S. Department of Labor.[15] It provides detailed information on more than 900 jobs gathered through a two-stage sampling involving a random sample of businesses, and within these, a random sample of workers in the target occupations. Data are gathered on many different aspects of each job, including physical exposures, based on responses by the sampled workers. O*NET has been used to construct job exposure matrices for a wide range of different occupational exposures.[16]

We used the O*NET survey item ‘‘Handling and Moving Objects,’’ which is measured on a seven-point scale (1 = low and 7 = high), and the scale is anchored with descriptors as follows: a score of 2 represents the effort involved in ‘‘changing settings on copy machines’’; 4 represents ‘‘arranging books in a library’’; and 6 represents ‘‘loading boxes on an assembly line.’’

The mean O*NET lifting score of all participants' jobs was 3.1. Jobs with O*NET scores greater than 3.5 were considered to involve regular manual work. These included, for example, patient handling in health care and most traditional ‘‘blue collar’’ jobs, while those with O*NET scores less than 3.5 included sales, office, management, business, science, and art occupations that involve little routine heavy lifting. Approximately 40% of participants had current jobs in the heavier lifting category.

Respondents were also asked about their own experience of lifting, pushing, and pulling in each job they held. Referring to large color photographs of a person lifting common household objects of various weights as a guide, participants chose one of three weight ranges for the heaviest object lifted regularly: 20 to 29 lbs (9.1 to 13.2 kg), 30 to 40 lbs (13.6 to 18.1 kg) or more than 40 lbs (>18.1 kg). For jobs that required them to carry loads of 20 lbs (9.1 kg) or more at least two to three times a day, they were asked to estimate the heaviest weight lifted on a regular basis in the same three categories. The typical daily amount of pushing and pulling on each job was also estimated on a 4-point Likert scale of frequency and a 5-point scale of effort, again assisted by photographs of a person ‘‘in action’’ pushing and pulling heavy objects.

Several different summary measures of occupational heavy lifting were constructed. To directly compare to the first case control study,[5] we combined all reported jobs for each person and calculated a variable—‘‘Cumulative Lifting Score’’ (weight x frequency x - years) for each respondent. The lifetime ‘‘Duration of Heavy

Lifting'' at work was calculated as the total number of years in jobs in which a participant reported regularly lifting more than 40 lbs (18.1 kg). We also created a binary variable (''Current Heavy Lifting'') that identified current jobs, which involved regular lifting of 30 lbs (13.6 kg) or more, (there were insufficient data to use the highest category of >40 lbs for this variable). Retirees were included in the reference category for this variable unless they had retired within the previous year, in which case the exposure reported for their last job was used. Current heavy lifting was identified, *a priori*, as the summary exposure measure corresponding to our primary hypothesis about the timing of relevant exposure.

Nonoccupational Lifting

Nonoccupational lifting activities, including housework, yardwork, sports, and hobbies, were assessed from self-reports. Two raters independently reviewed the answers to detailed questions on the frequency and intensity of nonoccupational lifting and strenuous activities. They scored two dichotomous variables, coding regular ''Non-occupational Lifting'' and ''Non-occupational Strenuous Activities'' into high versus low categories. When their independent ratings differed, they conferred and reached a consensus decision. ''High'' Non-occupational Lifting was defined as regular activities that raters judged involved frequent lifting of objects weighing at least 20 lbs (9.1 kg), such as carrying laundry up and downstairs, moving furniture, shoveling snow, and weight lifting. The raters coded ''High'' nonoccupational strenuous activities for participants who reported frequently getting out of breath or working up a sweat during housework, yardwork, sports, and hobbies. Common activities included scrubbing floors, raking leaves, mowing the lawn, and running.

Statistical Analyses

Descriptive statistics were analyzed using Chi-square tests and t-tests, as appropriate. We used smoothing splines to investigate the nonparametric relationships between age, BMI, continuous measures of physical activity, and risk of RDs and tears.[17] Multiple logistic regression modeling was used to assess the associations between case–control status and risk factors. Initial analyses found that RDs and RTs had very similar risk factors (see Results), so the final analyses included both types of cases (the combined analyses use the abbreviation RD/T to indicate that both detachments and tears were studied together). Model comparisons were based on the AIC.[12]

Propensity Score Matching

After initial multiple logistic regression models revealed a number of strong risk factors, and descriptive analyses showed complex correlations among these variables, we turned to propensity score matching to provide tighter control over multiple confounders and potential selection bias in models evaluating the hypothesis of the risk from occupational lifting. The first step in using propensity scores was to construct a logistic regression model to predict the probability of an individual being exposed, within the control population.[18] Candidates for predictors were all eight factors found in initial univariate logistic regression models to be associated with RD/T, as well as their two-way interactions. The fully saturated model with eight main effects and 28 two-way interactions did not converge, so we reduced this model, dropping product terms, until we found the best-fitting model for predicting the exposure variable of *a priori* interest, Current Heavy Lifting. This model included all eight main effects and 18 two-way interactions.

Once the model predicting the dichotomous exposure had been built using data for the controls, individual predicted probabilities of exposure were assigned to all cases and controls. The strength of the propensity score method is that, because the propensity score was constructed using all measured potential confounders and their interactions, the comparison of risk between exposed and nonexposed subjects with closely matched propensity scores provides a close approximation to a randomized experiment, comparing subjects who are as similar as possible on all measured confounders.[19]

Each exposed subject was matched (using Greedy Matching in SAS Procedure PSMatch) to up to three unexposed subjects with the closest propensity scores. Matched sets never differed by more than 0.25 of the standard deviation of the propensity scores as recommended by Rosenbaum and Rubin.[20] Rarely, three unexposed subjects did not meet this criterion in which case only two or one were selected. For the exposure of a priori interest, Current Heavy Lifting, 80% of matched sets included three unexposed, 10% included two and 10% included only one unexposed subject. Conditional logistic regression (SAS Procedure PHReg) was then used to calculate the hazard ratio (equivalent to the conditional OR in these case control data) for risk of RD/T from the dichotomous exposure variable within propensity score matched sets. We repeated this procedure with each of four different exposure metrics.

RESULTS

Two hundred nine cases and 425 controls completed the survey. Participation rates were approximately 73% in cases and 54% in controls. All but 13 participants completed the survey by mail, the rest by telephone. We excluded a total of nine potential cases and 10 controls because they did not meet inclusion criteria. Most omitted cases were diagnosed with retinal holes rather than RD/T and the majority of omitted controls reported a past history of RD/T.

We collected complete data on 200 cases of RD ($n = 105$) or RT ($n = 95$). About half of these ($n = 113$) were drawn from the central Massachusetts health care system, and the rest from the independent retinology practices in the same catchment area. We also gathered data on 415 controls, from patients visiting ophthalmology/optometry clinics for routine eye examinations (Table 1).

Participants were predominantly white (controls 87%, cases 93%), which is consistent with the central Massachusetts population. Cases were somewhat more likely to be male (55% of cases vs 36% of controls). As expected, cases were older on average than controls (61 vs 54 years, respectively). We observed a nonlinear shape of the relationship between age and RD/T (Fig. 1). The risk of RD/T rose steadily from young adulthood and peaked at about age 65, after which it declined rapidly through at least age 80. We investigated several ways to represent this nonlinear relationship in our multiple logistic regression models, including a three-category class variable, a spline, and a quadratic form using linear and squared terms. These three forms all fit similarly and here we report results from the quadratic parameterization.

Among myopics, we found almost a three-fold increase in risk of RD and only a weak increase in risk of RT compared to non-myopics (Table 2). Subanalyses restricted to participants for whom we had refractive error data to define myopia showed a very similar association with risk of RD/T. Also, controlling for confounding by myopia measured with refractive error rather than self-report had similar effects on other risk factors, suggesting that the self-reported measure was not introducing bias into the multivariable models.

Previous cataract surgery (in the same eye) greater than three months before RD/T was a strong risk factor for both RD and RT, although the magnitude of the effect was somewhat stronger for RD than for RT (OR = 10.4, 95% CI 4.8 to 22.1) and (OR = 6.5, 95% CI 2.7 to 15.4), respectively (Table 2). Family history of a close relative with RD/T was associated with more than a two-fold increase in risk of RD/T.

Increasing BMI was associated with *lower* risk of both RD (OR = 0.94, 95% CI 0.89 to 0.98) and RT (OR = 0.93, 95% CI 0.89 to 0.98). This negative association was unanticipated because the

TABLE 1. Demographic Characteristics, Cases of Retinal Detachment/Tear (RD/T), and Normal Controls

	Controls N, (%)	Cases of RD/T N, (%)	Test of Difference*
Total	**415**	**200**	**–**
Age, years			
18–49	37%	12%	
50–64	34%	51%	$P < 0.001$
65–69	11%	20%	
70+	18%	17%	
Gender			
Female	64%	45%	$P < 0.001$
Male	36%	55%	
Race			
White	87%	93%	$P = 0.02$
Nonwhite	13%	7%	
Education			
High school or less	35%	26%	
Trade school/College	45%	45%	$P = 0.01$
More than college	20%	29%	
Household income			
<$25,000	20%	9%	
$25,000–$49,000	23%	22%	$P = 0.01$
$50,000–$100,000	29%	32%	
>$100,000	28%	37%	
Smoking status			
Never	62%	65%	$P = 0.48$
Ever	38%	35%	
Alcohol consumption			
Never	37%	29%	
Sometimes	55%	58%	$P = 0.03$
Everyday	8%	13%	
Body mass index			
<18.5	1%	1%	
18.5–24.9	30%	35%	$P = 0.03$
25–29.9	33%	39%	
30+	36%	25%	
Myopia†			
No	54%	44%	$P = 0.02$
Yes	46%	56%	
Family history			
No	87%	71%	$P < 0.001$
Yes	13%	29%	
Cataract surgery‡			
No	93%	73%	$P < 0.001$
> 3 months ago	7%	27%	
Hypertension medication			
No	66%	54%	$P = 0.01$
Yes	34%	46%	

*P-value testing H_0: no difference between cases and controls, χ^2 test.
†Myopia defined as wearing glasses for distance vision starting by age 20 (see text).
‡Cataract surgery: EMR or self-report of previous cataract surgery in the same eye.

two previous studies reported positive associations.[5,7] We investigated the hypothesis that the negative BMI – RD/T association might be a secondary effect of a disproportionately high prevalence of diabetics among the controls (in this insured population, diabetics may be more likely to have regular eye examinations, and tend to be overweight). We therefore restricted the analysis to nondiabetics, and found that the negative BMI – RD/T association was of similar magnitude, but with wider CI (OR = 0.96, 95% CI 0.92 to 1.00), suggesting that the negative BMI – RD/T association was not fully explained by diabetes.

Physical Exertion

We found no evidence that nonoccupational heavy physical exertion increased risk of RD/T. The ORs for heavy Current Non-occupational Lifting (OR = 1.02, 95% CI 0.64 to 1.60) and Current Non-occupational Strenuous Activities (OR = 0.76, 95% CI 0.51 to 1.14) were essentially null.

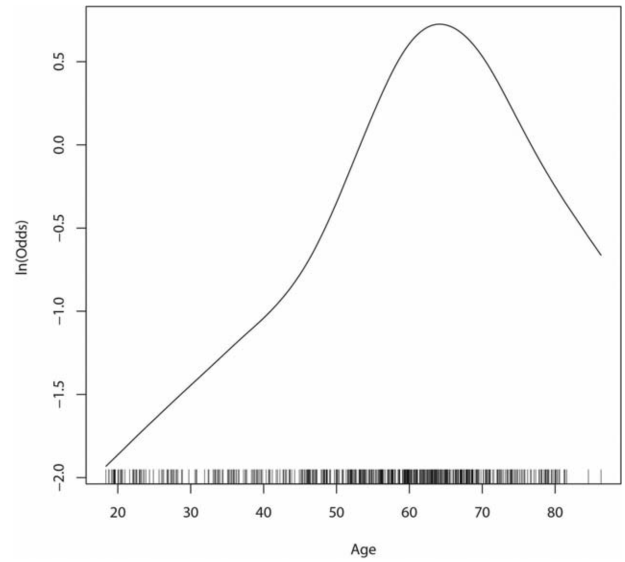

FIGURE 1. Spline curve showing the nonparametric relationship between age and risk of RD/T, expressed as the log of the odds ratio. The ''rug'' along the x-axis indicates the ages of the study population.

The strongest evidence for an association between occupational heavy lifting exposure and RD/T was found for the dichotomous exposure Current Heavy Lifting (Table 3). In the best-fitting model including this variable, the OR was 1.38, but the CI was wide and included the null (95% CI = 0.77 to 2.50). Restricting this analysis to those aged less than 65 years who were likely to have a current job, only modestly increased the strength of the association, with the same wide CI. No other exposure variables, including measures of lifetime cumulative exposure and lifetime duration of heavy lifting, showed any evidence for increased risk of RD/T (Table 2). Measures of pushing and pulling were similarly not associated with risk (data not shown).

The first report of an association between heavy lifting and RD[5] was among myopics. We therefore restricted our analyses to myopics, and found very similar results for the measures of physical exertion, albeit with wider CIs. This was true both for RD and RT separately, and together (data not shown).

Propensity Score Matching

It is likely that heavy lifting at work is associated, in complex nonlinear ways, with many of the other strong predictors of RD/T: age, gender, BMI, myopia, family history, and cataract surgery. Furthermore, these associations are likely to be time-dependent—changing both over calendar time as jobs have changed over the last 40 years, and as participants have aged. We used propensity score matching to provide tighter control over this complex pattern of interacting predictors than is possible with multiple regression models.

For each of the occupational exposure variables in Table 3, we modeled propensity scores as described above, and estimated the OR for risk of RD/T from propensity score matched sets with a 3:1 ratio of unexposed to exposed participants. Only one of the four exposure metrics was associated with RD/T – Current Heavy Lifting (OR = 1.62, 95% CI = 1.02 to 2.57) (Table 3). This metric is more meaningful for those who are young enough to be in the

TABLE 2. Important Determinants of Retinal Detachment/Tear

	All Cases (RD/T)†		RD Only†		RT Only†	
Covariate	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Age	1.30	1.16–1.44	1.18	1.06–1.32	2.58	1.75–3.80
Age squared	0.998	0.997–0.999	0.999	0.997–1.00	0.992	0.989–0.996
Male gender	2.14	1.44–3.18	2.73	1.63–4.58	1.90	1.13–3.20
Myopia‡	1.84	1.23–2.75	2.80	1.65–4.76	1.26	0.75–2.13
Cataract surgery§	6.81	3.62–12.82	10.35	4.84–22.11	6.46	2.71–15.44
Family history‖	2.44	1.50–3.99	2.92	1.60–5.32	2.24	1.18–4.24
BMI	0.94	0.90–0.97	0.94	0.89–0.98	0.93	0.89–0.98

Results of multiple logistic regression models*.

95% CI, 95% confidence interval; BMI, body mass index, OR, odds ratio; RD, retinal detachment; RD/T, retinal detachment or tear; RT, retinal tear; kg/m2 from self-reported height and weight.

*Each model includes all seven listed covariates. Other covariates that did not improve fit of All Cases model have been omitted.

†RD/T: outcome is RD and RT (model included 189 cases and 396 controls), RD: retinal detachment (99 cases and 396 controls), RT: retinal tear (90 cases and 396 controls).

‡Myopia defined as regularly wearing glasses before age 20 (see text).

§Cataract surgery = EMR or self–report of cataract surgery in the same eye.

‖Family history = self–report of first or second-degree relative with RD.

active workforce, and so we also restricted this model to the population under 65. The OR increased to 1.81, 95% CI = 1.08 to 3.04, or an 81% higher risk of RD/T for those with a current job involving heavy lifting, compared with no heavy lifting.

DISCUSSION

Although the diagnosis and treatment of RD/T are highly developed and generally effective, there has been relatively little research on primary prevention. We identified seven different risk factors for RD/T, with various implications for prevention.

Age is a well-known and strong risk factor for both RD and RT; however, the nonlinear shape of the relationship and the strong decline in risk after about age 65 is striking (Fig. 1). Others have also observed this pattern,[1] but we are not aware of a definitive explanation for the decline. Male gender is also a well-known risk factor for RD. Trauma has been suggested as one explanation for the higher rate in men, but it is also possible that heavy physical work could play a role.

Myopia had the expected strong effect on risk of RD/T, although some previous studies suggest an even stronger risk.[3] We think that it is likely that the myopia effect has been somewhat attenuated here because of our proxy measure, which probably contained some nondifferential misclassification. Despite this, we found no evidence that the proxy measure introduced confounding into the associations between RD/T and the other risk factors. The effect of myopia was the one association that appeared to differentiate RD from RT—there was a much stronger association of myopia with RD than RT (Table 2). We are not aware of explanations for this difference.

Previous cataract surgery was a very strong risk factor, as has been previously reported.[21] In designing the study, we tried to avoid this complicating factor by excluding participants who had cataract surgery within 3 months before their RD/T (or routine eye examination for controls). But the results in Table 2 show clearly that previous cataract surgery (in the same eye) was a strong risk factor even after excluding recent (within 3 months) cases. We did not have complete data on the date of cataract surgery in the records available for abstracting, and so we could not investigate the persistence of this risk over time or evaluate whether or not myopia (or other risk factors) increase this risk. This would be important to investigate further in a future study.

A family history of a close relative with RD also appeared to be a risk factor. It is possible that this might have been affected somewhat by recall bias, with cases more likely to remember or be aware of RD in the family. But a family history risk has also been reported by other investigators.[22]

We did not expect to find a negative association of BMI and RD/T, as both previous studies investigating this found positive associations.[5,7] We do not know what might account for this difference, although it may be important to note that the Italian

TABLE 3. Results of Alternative Models for Risk of RD/T Using Four Different Measures of Occupational Physical Exertion

	Multiple Logistic*		Propensity Score Matched†	
Exposure Metric†	**OR**	**95% CI**	**OR**	**95% CI**
Cumulative lifting score ‡	0.81	0.52–1.26	1.02	0.73–1.43
Number of years lifting > 40 lb	1.15	0.56–2.36	1.02	0.61–1.72
Current manual job	0.86	0.54–1.36	0.89	0.62–1.27
Current heavy lifting§	1.38	0.77–2.50	1.62	1.02–2.57
Among those ≤65 years				
Current heavy lifting	1.44	0.74–2.79	1.81	1.08–3.04

95% CI, 95% confidence interval; BMI, body mass index; OR, odds ratio; RD/T, retinal detachment or tear.

*All models adjusted for age, age^2, gender, myopia, cataract surgery, BMI, family history.

†See text for definitions.

‡Units: lbs/week-years. Cutoff was 15,653 (7100 kg-years), the median of the nonzero values.

§Regularly lifting > 30 lbs (13.6 kg) in current job.

and Swedish populations had much lower distributions of BMI, with few "overweight" or "obese" (BMI >25 and >30, respectively). Among our controls, 69% were overweight or obese versus 7% and 26% in the Swedish and Italian study populations, respectively.

The study by Mattioli et al[5] mentioned previously was the first epidemiologic study linking heavy lifting to risk of RD. A second epidemiologic study also found evidence that physical exertion, and specifically heavy lifting at work was associated with an increased risk of RD.[5,23] The second study was conducted in a cohort of approximately 49,000 Swedish men born in 1949 to 1951, enrolled during their compulsory military service in 1969 to 1970 and followed up to 2009 when they were about 60 years old. Heavy lifting was determined from their occupations in 1990, when they were about 40 years old. Those in occupations requiring lifting of heavy loads (> 20 kg or >44 lbs) at least twice/week had about twice the risk of RD compared to those in the lowest lifting category (relative risk = 2.38, 95% CI 1.15 to 4.93).

In designing the present case–control study to follow up the initial observation of Mattioli, we found it useful to develop explicit hypotheses about the causal mechanisms by which physical exertion might cause RD. In particular, the choice of how to summarize data on exposure—heavy lifting—is dependent on assumptions about the timing of exposure, and whether the effect is cumulative and gradual or acute and rapid.[24]

It is known that physical exertion causes rapid transient increases in intraocular pressure (IOP), providing a possible link between macro physical activities and intraocular dynamics,[25–27] but how transient increases in IOP might lead to RD is not known. One possible mechanism involves disruption of an evolving posterior vitreous detachment (PVD). RD is most common during the fifth through seventh decades[1] (Fig. 1), when PVD is also occurring in many eyes, and "anomalous" PVD may represent a frequent pathway to RD.[10] During a normal PVD, the vitreous shrinks and its cortex pulls away from the retina without damage. But if the vitreous liquefaction and shrinkage are not synchronized with weakening of vitreoretinal adhesion, a RT may occur.

We hypothesized that short-term peaks in intraocular pressure caused by heavy lifting occurring when an eye is going through PVD can disrupt the normal process, increasing the risk of an RT or RD. A rapid increase in IOP may force apart the vitreous cortex from the retina leading directly to a tear. If this hypothesis is correct, an epidemiologic study should find an association between lifting shortly before the RD and risk. It further follows that risk would be associated with the *current* job, during or shortly before the event, while exposures in the distant past would not be important, nor would the cumulative exposure over the entire career, except to the extent that a person's job characteristics may be very similar over her/his career.

The finding that risk of RD is modestly increased among those whose current job involved regular heavy lifting is consistent with this hypothesis, as is the lack of an association between cumulative exposure measures and RD risk. Many (27%) of our participants were retired, and so they had no "current" job. When we restricted the analysis to those under age 65, we found a stronger association between current heavy lifting and RD risk, providing further evidence for the hypothesis. We believe that the stronger association observed in the propensity score matched data was due to this method providing tighter control for the other strong covariates and their interactions than is possible in multiple logistic regression.

There are several potential limitations. First, our study relied on self-reported information for important covariates, including myopia, previous cataract surgery, and history of physical exertion. Regarding the prior hypothesis about the risk from heavy lifting, this study was also limited by the fairly low prevalence of occupational heavy lifting in this population; only 12.2% of the controls and 14.8% of cases reported regularly lifting 30 lbs (13.6 kg) or more in their current job. This is probably due to the types of industries present in the catchment area of central Massachusetts. Future investigations of the role of physical exertion in RD should focus on populations with a higher prevalence of heavy labor. It is possible that cases over-reported their history of physical exertion because of their belief that this may have been the cause of their RD/T. We are doubtful that this might fully explain the findings for two reasons. First, we might expect this recall bias to extend to nonoccupational lifting such as housework, yard work, and hobbies, but we did not find any evidence for an association between these and risk of RD/T. Second, the last item on the survey given to cases was an open-ended question: "Can you think of anything that may have caused your retinal detachment or retinal tear?". Only 40% of cases provided an opinion, the most common responses were various eye health conditions (11%), and references to heavy exertion or lifting were given by only seven cases (4%).

Caution is warranted in interpreting CIs in Table 3 because there were multiple different exposure variables evaluated. However, as noted above, the exposure metric with the strongest evidence of association corresponded to our primary *a priori* hypothesis on the timing of exposure and we believe this consistency should be borne in mind when evaluating the findings.

The present study and the two previous studies of lifting and RD risk[5,23] used different measures of occupational heavy lifting exposure. Unfortunately, neither of the two previous studies reported lifting data on the current job. The Italian case–control study by Mattioli et al[5] found RD risk to be associated with lifetime cumulative lifting exposure,[5] and the Swedish cohort study by Farioli et al[23] used a measure of occupational lifting for a time point early in participants' working lives. Our study did not find increased risk of RD/T with measures of lifting designed to be comparable in timing to either of the two previous studies. Thus, further research is needed on the timing of exposure and risk.

This study was not large enough to detect risk from specific nonoccupational activities such as weight lifting, which were reported by only a few subjects. Thus, the lack of evidence for these activities increasing risk may be simply because of insufficient statistical power.

In conclusion, there are potentially important risk factors for RD/T that need further investigation. The possibility that BMI affects risk, whether positively or negatively, has important implications for public health and the contradictory results of this and previous studies should be resolved. The modest elevation in risk we observed among those with current jobs involving heavy lifting requires further study in populations with a higher prevalence of heavy work and more accurate biomechanical exposure data.

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REFERENCES

1. Mitry D, Charteris DG, Yorston D, et al. The epidemiology and socioeconomic associations of retinal detachment in Scotland: a two-year prospective population-based study. *Invest Ophthalmol Vis Sci*. 2010;51:4963–4968.
2. Ghazi NG, Green WR. Pathology and pathogenesis of retinal detachment. *Eye (Lond)*. 2002;16:411–421.
3. Mitry D, Charteris DG, Fleck BW, Campbell H, Singh J. The epidemiology of rhegmatogenous retinal detachment: geographical variation and clinical associations. *Br J Ophthalmol*. 2009;94:678–684.
4. Pastor JC, Fernandez I, Rodriguez de la Rua E, et al. Surgical outcomes for primary rhegmatogenous retinal detachments in phakic and pseudophakic patients: the Retina 1 Project–report 2. *Br J Ophthalmol*. 2008;92:378–382.

5. Mattioli S, De Fazio R, Buiatti E, et al. Physical exertion (lifting) and retinal detachment among people with myopia. *Epidemiology*. 2008;19:868–871.
6. Alves C, Penedones A, Mendes D, Batel Marques F. A systematic review and meta-analysis of the association between systemic fluoroquinolones and retinal detachment. *Acta Ophthalmol*. 2016;94:e251–e259.
7. Farioli A, Hemmingsson T, Kriebel D. Vascular risk factors and rhegmatogenous retinal detachment: a follow-up of a national cohort of Swedish men. *Br J Ophthalmol*. 2016;100:907–913.
8. Curti S, Coggon D, Baldasseroni A, et al. Incidence rates of surgically treated rhegmatogenous retinal detachment among manual workers, non-manual workers and housewives in Tuscany, Italy. *Int Arch Occup Environ Health*. 2014;87:539–545.
9. Curti S, Coggon D, Hannerz H, Mattioli S. Heavy lifting at work and risk of retinal detachment: a population-based register study in Denmark. *Occup Environ Med*. 2016;73:51–55.
10. Sebag J. Anomalous posterior vitreous detachment: a unifying concept in vitreo-retinal disease. *Graefes Arch Clin Exp Ophthalmol*. 2004;242:690–698.
11. Cumberland PM, Chianca A, Rahi JS, Eye UKB, Vision C. Accuracy and utility of self-report of refractive error. *JAMA Ophthalmol*. 2016;134:794–801.
12. Akaike H. A new look at the statistical model identification. *IEEE Trans Automatic Control*. 1974;19:716–723.
13. O*NET. About O*NET. http://www.onetcenter.org/overview/html. Accessed September 18, 2019.
14. O*NET. O*NET Resource Center-Overview. Available at: http://www.onetcenter.org/. Accessed October 30, 2019.
15. O*NET. O*NET Online Database. Available at: https://www.onetonline.org/help/onet/database. Accessed October 30, 2019.
16. Cifuentes M, Boyer J, Gore R, et al. Inter-method agreement between O*NET and survey measures of psychosocial exposure among healthcare industry employees. *Am J Ind Med*. 2007;50:545–553.
17. Hastie TJTR. *Generalized Additive Models. Vol 43*. New York: Chapman & Hall/CRC; 1990.
18. Mansson R, Joffe MM, Sun W, Hennessy S. On the estimation and use of propensity scores in case-control and case-cohort studies. *Am J Epidemiol*. 2007;166:332–339.
19. Joffe MM, Rosenbaum PR. Invited commentary: propensity scores. *Am J Epidemiol*. 1999;150:327–333.
20. Rosenbaum PR, Rubin DB. Constructing a control group using multivariate matched sampling methods that incorporate the propensity score. *Am Stat*. 1985;39:33–38.
21. Olsen T, Jeppesen P. The incidence of retinal detachment after cataract surgery. *Open Ophthalmol J*. 2012;6:79–82.
22. Mitry D, Singh J, Yorston D, et al. The predisposing pathology and clinical characteristics in the Scottish retinal detachment study. *Ophthalmology*. 2011;118:1429–1434.
23. Farioli A, Kriebel D, Mattioli S, Kjellberg K, Hemmingsson T. Occupational lifting and rhegmatogenous retinal detachment: a follow-up study of Swedish conscripts. *Occup Environ Med*. 2017;74: 489–495.
24. Smith TJ, Kriebel D. *Biologic Approach to Environmental Assessment and Epidemiology*. New York: Oxford University Press; 2010.
25. Hagins M, Pietrek M, Sheikhzadeh A, Nordin M. The effects of breath control on maximum force and IAP during a maximum isometric lifting task. *Clin Biomech (Bristol Avon)*. 2006;21:775–780.
26. Narloch JA, Brandstater ME. Influence of breathing technique on arterial blood pressure during heavy weight lifting. *Arch Phys Med Rehabil*. 1995;76:457–462.
27. Vieira GM, Oliveira HB, de Andrade DT, Bottaro M, Ritch R. Intraocular pressure variation during weight lifting. *Arch Ophthalmol*. 2006;124: 1251–1254.